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Questa è la Versione finale referata (Post print/Accepted manuscript) della seguente pubblicazione:

Original Citation:

Primary cutaneous CD30+ T-cell lymphomas: hypothesis for a highly distinctive clinicobiological behaviour / Pimpinelli N. - In: JOURNAL OF THE EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY. - ISSN 0926-9959. - STAMPA. - 15(2001), pp. 108-109.

Availability:

This version is available at: 2158/771666 since:

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Primary cutaneous CD30+ T-cell lymphomas: hypothesis for a highly distinctive clinicobiological behaviour

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Pedrajas A, Velez A, Jiménez A *et al.* Lymphoma *en cuirasse*. *JEADV* 2001; **15**: 186–187.

In this issue a case of CD30+ non-Hodgkin's lymphoma (NHL) involving the skin with *en cuirasse* clinical features (large, indurated, well-defined plaque of the breast, simulating a carcinoma 'en cuirasse') is reported (see pp. 000–000). This report is definitely worthy of attention for its clinical peculiarity. On this occasion, however, it seems advisable to stress once again the usual, distinctive features of primary cutaneous CD30+ T-cell lymphomas (CD30+ CTCLs), and to discuss the hypothetical mechanism(s) underlying the most distinctive clinical feature of this cutaneous lymphoma subtype, i.e. the spontaneous regression of skin lesions.

CD30+ CTCL represents a well-defined, specific subtype of NHL with a primary cutaneous presentation.¹ Key features are: the expression of CD30 antigen by neoplastic large cells at presentation; the possible spontaneous regression of skin lesions; and the generally favourable clinical course. This distinctive CTCL subtype includes a spectrum of diseases known as CD30+ lymphoproliferative disorders of the skin:^{2,3} primary cutaneous CD30+ large T-cell lymphoma (CD30+ large cell CTCL), lymphomatoid papulosis (LyP), and so-called 'borderline' cases. CD30+ large cell CTCL are characterized clinically by presentation with solitary or localized skin lesions, possible spontaneous regression (partial to complete), good and rapid response to local radiotherapy, and favourable prognosis, despite frequent cutaneous relapses. Histologically, they comprise a skin infiltration of large T cells, > 75% of which express CD30 antigen, regardless of their predominant cytology, i.e. anaplastic (anaplastic large cell, ALC) or non-anaplastic (pleomorphic, immunoblastic).⁴ LyP, historically defined as 'a continuing, self-healing eruption, clinically benign, histologically malignant',⁵ is characterized clinically by an intermittent or continuous eruption of usually multiple, papulonodular lesions, with ulceration, crusting and self-healing, sometimes with scarring and/or depigmentation. Histologically, three main patterns are recognized (reviewed in Willemze *et al.*¹): (i) LyP type A, i.e. large atypical CD30+ cells, scattered or in small clusters, are interspersed in an extensive inflammatory

infiltrate of histiocytes, small lymphocytes, neutrophils and/or eosinophils; (ii) LyP type B, i.e. medium-sized cerebriform cells are arranged in a perivascular to band-like, epidermotropic infiltrate, simulating classical plaque stage MF; and (iii) LyP type C, i.e. monotonous infiltration or large clusters of CD30+ T cells with relatively few admixed inflammatory cells, resembling CD30+ large cell CTCL. Different histological types of LyP may occur in different lesions, or part of the same lesion, of individual patients. 'Borderline' cases are characterized by clinical features typical of large cell lymphoma with histology of LyP, or vice versa.³

Although the functional relevance of CD30 and its natural ligand (CD30L) expressed in most NHL is presently not known, previous studies indicate that CD30L is likely to mediate the reduction of proliferation in CD30+ ALC NHL.⁶ No information was available concerning the expression of CD30L in primary cutaneous CD30+ lymphomas. We investigated the immunophenotypic and genotypic expression of CD30 and CD30L in different developmental phases of skin lesions (growing vs. spontaneously regressing). By immunohistochemistry, CD30L expression was detected in regressing lesions only; by molecular analysis, the expression of CD30L was clearly higher in regressing lesions than in growing ones. CD30L, while expressed by some small lymphocytes, was most often coexpressed by CD30+ neoplastic large cells, as demonstrated by two-colour immunofluorescence and by immunohistochemistry on paraffin sections. Taken together, these data suggest that CD30–CD30L interaction may play a part in the pathobiology of primary cutaneous CD30+ lymphoproliferative disorders.⁷ Indeed, CD30L expression by both neoplastic and reactive cells, possibly enhancing the tumour cell sensitivity to FasL-mediated cell death might represent the triggering mechanism for apoptosis, which is frequent in regressing lesions.⁸ The lack of activation of specific oncogenes (low levels of bcl-2 in LyP regressing lesions, different from CD30+ large cell tumours)⁹ and the presence of active receptors for transforming growth factor- β , a potent growth inhibitor of normal lymphocytes^{10,11} are possible prerequisites for the success of the above, putative role of CD30–CD30L interaction.

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